REMARKS

Claim 1-20, 24-37 and 43-48 are now in the application. Claims 1-20 and 24-37 are drawn to the elected invention. Claim 43-48 are drawn to non-elected invention and may be canceled by the Examiner upon the allowance of the claims drawn to the elected invention.

Claims 1-20 and 24-37 were rejected under 35 U.S.C.103 (a) as being unpatentable over U.S. Patent 4,751,221 to Watanabe et al. (hereinafter referred to as "Watanabe"). Watanabe does not render obvious Claims 1-20 and 24-37.

Claims 1-20 and 24-37 relate to improved methods for synthesizing 2-chloro-9-(2-deoxy-2fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine [clofarabine] wherein the anionic form of a 2-chloro-6-substituted-purine is reacted with a protected and activated 2-deoxy-2-fluoro-D-arabinofuranose followed by reacting with an appropriate base such as ammonia to provide 2-chloro-9-(2-deoxy-2-fluro-β-D-arabinofuranosyl)-9*H*-purin-6-amine. The reported method for synthesizing 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine resulted in low overall yields of product, typically in the range of about 13%. The described coupling reaction produced a mixture of nucleosides from which the desired 9-β intermediate was obtained in only 32% yield after careful chromatography. Direct amination/deprotection of this material gave the desired 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine, plus a partially benzoylated 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine that required further base treatment. Pure 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine was obtained only after several re-crystallizations were carried out to remove salts and residual benzamide.

Such inefficient reactions will inhibit the ability to commercially produce 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine. As discussed in the Specification, the present invention provides improved methods for synthesizing 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine that results in increased yields and/or reduced process steps.

Watanabe does not suggest or render obvious Claims 1-20 and 24-37 since, among other things, Watanabe does not even remotely suggest a reaction of a purine nucleoside having a 6-alkoxy group to obtain the desired final product. It is important to keep in mind that the present invention does not relate to producing final products having an alkoxy group at the C-6 position of the purine ring, but instead relates to producing 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine. Although, a number of suggested reaction schemes are reported by Watanabe (e.g.-see columns 3 and 4), no reaction scheme is suggested whereby a purine having a 6-alkoxy group is reacted to obtain the desired product. In fact, no reaction sequence is even provided by Watanabe to produce the 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine, the target compound of the process of the present claims.

Nothing in Watanabe would lead a person skilled in the art to react a purine having a 6-alkoxy group to obtain 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine with the expectation of achieving increased yields and/or reduced process steps as discussed in the specification. In other words, nothing in the cited art exists that suggests that by employing an extra process step as employed according to this invention, would be of significant benefit as discussed above. The desired product of the claimed process is more readily available as compared to prior art processes. This additional step according to the present invention is crucial to the process of the present invention.

The mere fact that cited art may be modified in the manner suggested by the Examiner does not make this modification obvious, unless the cited art suggests the desirability of the modification. No such suggestion appears in the cited art in this matter. The Examiner's attention is kindly directed to *In re Lee* 61 USPQ2d 1430 (Fed. Cir. 2002), *In re Dembiczak et al.* 50 USPQ2d.1614 (Fed.Cir. 1999), *In re Gordon*, 221 USPQ 1125(Fed. Cir. 1984), *In re Lasowski*, 10 USPQ2d 1397 (Fed. Cir. 1989) and *In re Fritch*, 23 USPQ2d.1780 (Fed. Cir. 1992).

In *Dembiczak et al.*, supra, the Court at 1617 stated: "Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine

prior art references. See, e.g., C.R. Bard, Inc., v. M3 Sys., Inc., 157 F.3d 1340, 1352, 48 USPQ2d. 1225, 1232 (Fed. Cir. 1998) (describing 'teaching or suggestion motivation [to combine]' as in 'essential evidentiary component of an obviousness holding'), In re Rouffet, 149 F.3d 1350, 1359, 47 USPQ2d. 1453, 1459 (Fed. Cir. 1998) ('the Board must identify specifically...the reasons one of ordinary skill in the art would have been motivated to select the references and combine them');..."

Also, the cited art lacks the necessary direction or incentive to those or ordinary skill in the art to render the rejection under 35 USC 103 sustainable. The cited art fails to provide the degree of predictability of success of achieving the results attainable by the present invention needed to sustain a rejection under 35 USC 103. See *Diversitech Corp. v. Century Steps, Inc.* 7 USPQ2d 1315 (Fed. Cir. 1988), *In re Mercier*, 185 USPQ 74 (CCPA 1975) and *In re Naylor*, 152 USPQ 106 (CCPA 1966).

Moreover, the properties of the subject matter and results which are inherent in the claimed subject matter and disclosed in the specification are to be considered when evaluating the question of obviousness under 35 USC 103. See *Gillette Co. v. S.C. Johnson & Son, Inc.*, 16 USPQ2d. 1923 (Fed.Cir. 1990), *In re Antonie*, 195, USPQ 6 (CCPA 1977), *In re Estes*, 164 USPQ 519 (CCPA 1970), and *In re Papesch*, 137 USPQ 43 (CCPA 1963).

No property or result can be ignored in determining patentability and comparing the claimed invention to the cited art. Along these lines, see *In re Papesch*, supra, *In re Burt et al*, 148 USPQ 548 (CCPA 1966), *In re Ward*, 141 USPQ 227 (CCPA 1964), and *In re Cescon*, 177 USPQ 264 (CCPA 1973).

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Application No.: 09/889,287 Docket No.: 21381-00067-US

In the event the Examiner believes an interview might serve to advance the prosecution of this application in any way, the undersigned attorney is available at the telephone number noted below.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 22-0185, under Order No. 21381-00067-US from which the undersigned is authorized to draw.

Dated: 3-7-05

Respectfully submitted,

By _____

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